

CLAIMS

I claim:

1. Isolated brain derived tissue not containing any physiologically active amounts of immunocompetent glial cells.
2. Said tissue described in claim 1, almost substantially consisting of dopaminergic neurons, cholinergic neurons, GABAergic neurons, and/or serotonergic neurons or differentiate into these neurons.
3. Said tissue described in claim 1, substantially consisting of dopaminergic neurons or cells that can differentiate into dopaminergic neurons.
4. Said tissue described in claim 1, substantially consisting of cholinergic neurons or cells that can differentiate into cholinergic neurons.
5. Said tissue described in claim 1, substantially consisting of GABAergic striatal neurons or cells that can differentiate into GABAergic striatal neurons.
6. Said tissue described in claim 1, substantially consisting of serotonergic neurons or cells that can differentiate into serotonergic neurons.
7. Said tissue described in claim 1, further characterized that the tissue is derived from mammals, especially humans.
8. Said tissue described in claim 7, further characterized that this is derived from developing immature (progenitor) cells.
9. Tissue that is useful to restore neuronal deficits after transplantation generated according to claim 1.
10. Monoclonal cell line derived from mammalian, especially human, progenitor cells characterized by exclusive or predominant differentiation into neurons when exposed to differentiation promoting factors.

11. Method to generate an expandable tissue culture derived from progenitor cells comprising the following individual steps:

dissection of mammalian brain tissue

isolation of progenitor cells

proliferation of progenitor cells

partial differentiation of progenitor cells

if necessary repetition of at least one of the steps isolation, proliferation and partial differentiation

12. Method according to claim 11, further characterized by selecting individual cells using subcloning

13. Said method described in claim 12, using one or multiple of the following procedures in suitable sequences:

subcloning using final dilution

subcloning using micromanipulation

subcloning using fluorescence activated cell sorting

subcloning using labeling and isolation with superparamagnetic beads.

14. Said method described in claim 11, further characterized by the fact that the selection and partial differentiation of progenitor cells may be performed in conditions with reduced or increased oxygen/ nitrogen content or conditions that simulate reduced or increased oxygen/nitrogen content.

15. Said method described in claim 12, further characterized by the fact that oxygen content is less than 10 %, preferably less than 5 %.

16. Said method described in claim 12, further characterized by the fact that the conditions induced by reduced oxygen content may be simulated by application of compounds such as inhibitors of mitochondrial energy production.

17. Said method described in claim 11, further characterized by the fact that the progenitor cells are partially differentiated using expression of foreign genes or priming.

18. Said method described in claim 11, further characterized by the fact that the progenitor cells are partially differentiated by priming using treatment with appropriate cytokines, growth factors, hormones, neurotransmitters, transcription factors and/or gangliosides for periods of time that induce expression of tissue specific genes but do not preclude proliferation.

19. Said method described in claim 18, further characterized by the fact that priming is induced by one or a combination of members of the following growth factor families: EGF, FGF, GDNF, TGF α and β , LIN-3-protein, NGF, BDNF, NT, PDNF, IGF and/or VEGF, including respective subunits.

20. Said method described in claim 18, further characterized by the fact that priming is induced by one or a combination of the following cytokines: LIF, CNTF, interleukines (IL1-16), interferones, MIF, MSF, retinoic acid.

21. Said method described in claim 18, further characterized by the fact that priming is induced by one or a combination of the following neurotransmitters: dopamine, acetylcholine, GABA, glutamate, glycine, taurine, proline, noradrenaline, serotonin, substance P, enkephaline.

22. Said method described in claim 18, further characterized by the fact that priming is induced in monoclonal progenitor cell lines.

23. Said method described in claim 11, further characterized by the fact that proliferation of progenitor cells is achieved under hypoxic conditions or addition of exogenous factors.

24. Tissue culture generated according to claim 18.

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25. Tissue capable of restoring neuronal deficits following transplantation generated according to claim 24.

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